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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,980	02/14/2001	Michael Eisenhut	41443	9550

7590

08/13/2002

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EXAMINER

SCHULTZ, JAMES

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 08/13/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/781,980

Applicant(s)

EISENHUT ET AL.

Examiner

J. Douglas Schultz

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☒ Claim(s) 4-18 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☒ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____

DETAILED ACTION

Claim Objections

Claims 4-18 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from a multiply dependent claim. See MPEP § 608.01(n). Accordingly, claims 4-18 have not been further treated on their merits.

Claims 17 and 18, while being improperly multiply dependent as outlined above and thus not examined, are noted as providing for the use of the claimed compounds, but, since the claims do not set forth any steps involved in the methods/processes, it is unclear what methods/processes applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Had these claims had been examined, said claims would have been rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 14 lists an 18-mer oligonucleotide. As per C.F.R. 1.821,

Patent applications which contain disclosures of nucleotide and/or amino acid sequences must contain, as a separate part of the disclosure, a paper or compact disc copy (see § 1.52(e)) disclosing the nucleotide and/or amino acid sequences and associated information using the symbols and format in accordance with the requirements of §§ 1.822 and 1.823. This paper or compact disc copy is referred to elsewhere in this subpart as the "Sequence Listing." Each sequence disclosed must appear separately in the "Sequence Listing." Each sequence set forth in the "Sequence Listing" must be assigned a separate sequence identifier. The sequence identifiers must begin with 1 and increase sequentially by integers. If no sequence is present for a sequence identifier, the code "000" must be used in place of the sequence. The response for the numeric identifier <160> must include the total number of SEQ ID NOs, whether followed by a sequence or by the code "000."

Thus, any nucleotide listing that appears in either the specification or the claims must be identified by Sequence Identifier Numbers, and the application as a whole must contain a separate sequence listing; correction is necessary before further search and examination may take place in regards to claim 14 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagy et al., in view of Lu et al. and Taylor et al.

Claims 1-3 are directed to an oligonucleotide conjugate comprising an oligonucleotide complexed with a somatostatin analog wherein said oligo is complementary to a cellular mRNA transcript, wherein the oligonucleotide may be an oligodeoxyribonucleotide, or wherein the oligo phosphodiester bonds are at least partially replaced by phosphorothioate linkages.

Nagy et al. teaches somatostatin analogs that are conjugated to cytotoxic compounds, wherein said somatostatin analogs are used to deliver said cytotoxic compounds to cause cell death in cells that express somatostatin receptors (see abstract, page 1796 para. 4, and pg. 1796, last para, to 1797). Nagy et al. does not teach said analogs conjugated to an oligonucleotide, modified or otherwise.

Lu et al. teaches compounds that are complexed to an oligodeoxyribonucleotide that is antisense to cellular transcripts. The compound of the conjugates of Lu et al. are used to target cells expressing receptors that recognize said compound, thereby delivering the attached oligodeoxyribonucleotide to specific cell types (see abstract, p. 273, para. 2, and discussion, particularly para. 1).

Taylor et al. teach that modification of antisense oligos, including the incorporation of phosphorothioate linkages into said oligos, confer a greater degree of resistance to nuclease-mediated-degradation (p. 562, para. 2 through p. 563).

It would have been obvious for one of ordinary skill in the art to substitute an antisense compound as taught by Lu et al. in place of the cytotoxic compound of the somatostatin analog conjugates as taught by Nagy et al. It also would have been obvious to one of ordinary skill in the art to incorporate phosphorothioate modifications into the antisense molecules of Lu et al.,

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because Taylor et al. teach that such modifications improve bioactivity half-life and cellular uptake of antisense molecules. One of ordinary skill in the art would have been motivated to do so because Nagy et al. teach that somatostatin conjugates can be used to deliver cytotoxic compounds to target cells that express the somatostatin receptor, which is abundantly expressed on many cancer cell types, and because Taylor et al. teach that phosphorothioated antisense oligos have shown promise in treating cancer in clinical trials. One of ordinary skill in the art would have had a reasonable expectation of success in formulating such conjugates, because Lu et al. teach their methods of synthesis, and because such conjugations are routinely performed by those of ordinary skill in the art. Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

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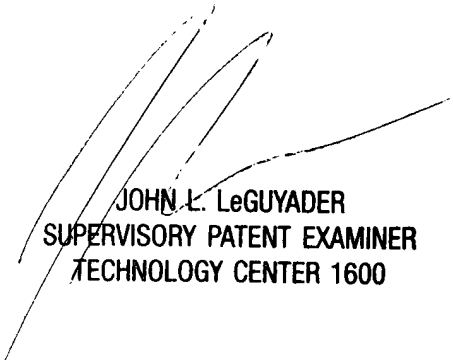
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 703-308-9355. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

J. Douglas Schultz, PhD
August 12, 2002



JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600